

### **Amendments to the Specification**

1. Please replace the paragraph describing Fig. 1A, 1B and 1C, beginning on line 11 of page 11, with the following amended paragraph:

**FIG. 1A, 1B, 1C. The Sequence and the Message of Fortilin.** **FIG 1A.** The amino acid sequence of human Fortilin (SEQ ID NO:2) was aligned to those of rabbit (SEQ ID NO:3), mouse (SEQ ID NO:4), chicken (SEQ ID NO:5), *Drosophila melanogaster* (*D. melanogaster*) (SEQ ID NO:6), *Caenorhabditis elegans* (*C. elegans*) (SEQ ID NO:7), *Saccharomyces cerevisiae* (*S. cerevisiae*) (SEQ ID NO:8) and rice (SEQ ID NO:9), using a sequence analysis program. Black and gray boxes represent amino acids that are identical and homologous to those of human Fortilin, respectively. The numbers within parentheses indicate GenBank accession numbers. **FIG. 1B.** The amino acid sequence of Fortilin was evaluated for its hydrophilicity. A peptide representing the 90<sup>th</sup>- 111<sup>th</sup> amino acids of Fortilin was used to raise antibody against Fortilin in rabbits. **FIG. 1C.** Northern hybridization was carried out on multiple tissue blots of adult human mRNA using a Fortilin cDNA probe. The  $\beta$ -actin cDNA probe was used to evaluate the amount of mRNA loaded in each lane. The Fortilin message was present ubiquitously in various human tissues, especially in the liver, kidney, small intestine, skeletal muscle, and testis.

2. Please replace the paragraph beginning at page 24, line 9, which starts with “Proteinaceous compositions may be made”, with the following amended paragraph:

Proteinaceous compositions may be made by any technique known to those of skill in the art, including the expression of proteins, polypeptides or peptides through standard molecular biological techniques, the isolation of proteinaceous compounds from natural sources, or the chemical synthesis of proteinaceous materials. The nucleotide and protein, polypeptide and peptide sequences for various genes have been previously disclosed, and may be found at computerized databases known to those of ordinary skill in the art. One such database is the National Center for Biotechnology Information's Genbank and GenPept databases (~~<http://www.ncbi.nlm.nih.gov/>~~ available on the World Wide Web at [ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov/)). The coding regions for these known genes may be amplified and/or expressed using the techniques disclosed herein or as would be known to those of ordinary skill in the art. Alternatively, various commercial preparations of proteins, polypeptides and peptides are known to those of skill in the art.

3. Please replace the paragraph beginning at page 85, line 9, which starts with "Host cells may be derived from prokaryotes", with the following amended paragraph:

Host cells may be derived from prokaryotes or eukaryotes, including yeast cells, insect cells, and mammalian cells, depending upon whether the desired result is replication of the vector or expression of part or all of the vector-encoded nucleic acid sequences. Numerous cell lines and cultures are available for use as a host cell, and they can be obtained through the American Type Culture Collection (ATCC), which is an organization that serves as an archive for living cultures and genetic materials (~~[www.atcc.org](http://www.atcc.org)~~ available on the World Wide Web at [atcc.org](http://www.atcc.org)). An appropriate host can be determined by one of skill in the art based on the vector

backbone and the desired result. A plasmid or cosmid, for example, can be introduced into a prokaryote host cell for replication of many vectors. Bacterial cells used as host cells for vector replication and/or expression include DH5 $\alpha$ , JM109, and KC8, as well as a number of commercially available bacterial hosts such as SURE<sup>®</sup> Competent Cells and SOLOPACK<sup>™</sup> Gold Cells (STRATAGENE<sup>®</sup>, La Jolla, CA). Alternatively, bacterial cells such as *E. coli* LE392 could be used as host cells for phage viruses. Appropriate yeast cells include *Saccharomyces cerevisiae*, *Saccharomyces pombe*, and *Pichia pastoris*.

4. Please replace the paragraph beginning at page 139, line 25, which starts with “Generation of anti-Fortilin antibody”, with the following amended paragraph:

**Generation of anti-Fortilin antibody:** Antiserum specific for Fortilin was prepared in rabbits using a synthetic peptide NH<sub>2</sub>-CKYIKDYMKSIKGKLEEQRPER-COOH (SEQ ID NO:10), corresponding to amino acids 90<sup>th</sup>-111<sup>th</sup> conjugated to maleimide-activated keyhole limpet haemocyanin (KLH) and an appropriate adjuvant. Generated antiserum was purified by affinity chromatography on a peptide-Sepharose matrix and tested by ELISA against a control or the Fortilin peptides.

5. Please replace the paragraph beginning at page 140, line 1, which starts with “Western blot of fusion proteins”, with the following amended paragraph:

**Western blot of fusion proteins:** The full length Fortilin cDNA was cloned in frame to pQE-30 bacterial expression plasmid (Qiagen, Valencia, CA). The plasmid was co-transformed

into BL21 *E.Coli* with pREP4 plasmid (Qiagen). The polyhistidine tagged Fortilin (MRGS-His<sub>6</sub>-Fortilin) was induced by addition of IPTG (isopropyl-β-D-thiogalactopyranoside), purified to near homogeneity under native conditions according to the manufacturer's instruction (Qiagen). The integrity of purified MRGS-His<sub>6</sub>-Fortilin was confirmed by SDS-PAGE (Polyacrylamide gel electrophoresis) and Coomassie staining, showing a single band at around 30kDa (Data not shown). For the characterization of the rabbit anti-Fortilin antibody, serially diluted RGS-His<sub>6</sub>-Fortilin (100ng to 12.5ng by weight), was subjected to SDS-PAGE and Western transfer. Transferred proteins were probed first with anti-RGS-His monoclonal antibody (Qiagen). The membrane was then stripped and re-probed with rabbit anti-Fortilin antibody. For the evaluation of the specificity of the antibody, a SDS-PAGE and Western transfer were performed in duplicate. Prior to the addition of antibodies, the membranes were pre-incubated either with a control peptide consisting of 210<sup>th</sup>-230<sup>th</sup> amino acid of MCL1 (NH<sub>2</sub>-LETLRVGDGVQRNHETVFQG-COOH) (SEQ ID NO:11) or with the Fortilin peptide (NH<sub>2</sub>-CKYIKDYMKSIKGGLEEQRPER-COOH) (SEQ ID NO:10) used to raise the antibody, both at a concentration of 100ng/mL. The rest of immuno-probing was performed as previously described (Kamitani *et al.*, 1997).

6. Please replace the paragraph beginning at page 166, line 21, which starts with “To determine which part of Fortilin”, with the following amended paragraph:

To determine which part of Fortilin was critical for binding with MCL1, various Fortilin deletion mutants were constructed and tested for their ability to interact with MCL1 in vitro. MCL1 interacted with full-length Fortilin (amino acids 1-172) and Fortilin<sub>Δ5-172</sub>, but not with

Fortilin $\Delta$ 23-172 or Fortilin $\Delta$ 46-172. The data suggested that the N-terminus amino acids 5-22 of Fortilin (RDLISHDEMFSDIYKIRE) (SEQ ID NO:12) was necessary for binding with MCL1 (Figure 14).